Schering-Plough

Thomas J. Sabatino, Jr.
Executive Vice President
and General Counsel

Schering-Plough Corporation
2000 Galloping Hill Road
Kenilworth, New Jersey 07033-0530
Telephone (908) 298-7367
Fax (908) 298-7555

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HHS Task Force on Drug Importation

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Schering-Plough is pleased to submit the following comments addressing several specific issues under consideration by the HHS Task Force on Drug Importation. We agree that providing affordable prescription drugs to our seniors represents an important public health need. We also support the prescription drug benefits provided under the Medicare Modernization Act of 2003 and believe that this coverage should enable seniors to receive access to safe and effective pharmaceutical products controlled under the most rigorous regulatory system in the world – that of the Food and Drug Administration.

Importation of prescription drugs is not a simple transaction between Canadian pharmacies or other online services and U.S. patients, but rather a complex process requiring rigorous regulatory safeguards to ensure safety, quality and efficacy. Without adequate safeguards provided by the FDA and U.S. Customs, the importation process has the potential for infiltration by substandard and counterfeit products. Schering-Plough is concerned the current proposal to implement an importation program will compromise the high standards U.S. citizens currently demand in our healthcare system while providing only a limited cost savings. In addition, we believe that it will have the significant consequence of negatively impacting innovation in pharmaceutical treatment.

THE IMPORTATION OF PHARMACEUTICALS WILL COMPROMISE THE SAFETY OF THE CURRENT U.S. DISTRIBUTION SYSTEM

The current drug distribution system in the United States has several key elements that apply to all legal prescription drugs - a label that identifies required storage conditions (such as controlled

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room temperature or refrigeration), an expected distribution chain (usually from licensed manufacturer to wholesaler to retailer to patient) and a presumption that they all share a desire to avoid contamination of the distribution chain with degraded or counterfeit products. Broad scale importation threatens the integrity of this system.

For example, if product were to be shipped first to an ex-U.S. wholesaler and then subsequently move into the U.S. supply chain, it is likely that the foreign wholesaler will not be subject to the same safeguards that are required of U.S. wholesalers. U.S. wholesalers are licensed by the state board of pharmacy in every state for which they are distributing products. These wholesalers are subject to inspections by the state board inspectors and are subject to a rigorous qualification process. These requirements help assure the safety of product in the supply chain. However, when products are allowed to be imported from multiple sources and unregulated wholesalers you lose the strong protections afforded by these stringent requirements.

Further, since the original manufacturer may not be considering that product for distribution within the U.S., that manufacturer will not be manufacturing or testing according to FDA standards. The implementation of an importation program must thus address the need for compliance with such standards, as well as how compliance will be monitored prior to a product's entry into the U.S. distribution chain. Without addressing these issues, FDA could not administer an importation program that assures the same level of quality provided by those FDA-approved products currently in the U.S. distribution chain.

IMPORTATION WILL PROVIDE FEW COST SAVINGS TO CONSUMERS OR THE HEALTHCARE SYSTEM AS A WHOLE

The European Union (EU) has had experience with State-sanctioned parallel trade of pharmaceuticals among EU member states. Parallel trade is permitted and even encouraged by Member states within the EU. Re-importation of prescription drugs within the EU was relatively modest before 2000, but since then has grown significantly as a share of the overall drug market in Europe. According to one source, reimportation accounted for 7 to 8 percent of the total prescription drug market in late 2001 and is expected to more than double in volume and account for 10 percent of the market by 2006.[1]

Only a few empirical studies have measured the actual impact of parallel trade on drug prices and the benefits to consumers and health insurers. In general, these studies have found that while parallel trade does exert a limited downward pressure on prices, patients realize little savings. Nearly all of the arbitrage between low prices in source countries and high prices in importing countries is absorbed by the parallel importers who are not investing those profits in further innovation. Only a small portion of the total "savings" is passed on to health insurers.

Parallel Traders Absorb Most of the Arbitrage from Parallel Trade

Most studies have concluded that the primary effect of parallel trade is to reallocate surpluses of pharmaceutical manufacturers to parallel traders. In theory, parallel traders are motivated to purchase brand name drugs where the spread in price of the drug between low price and high-

[1] The Global Parallel Trade Outlook 2001-2006, Reuters Business Insight 2001, p. 12; as quoted in Jacob Arfwedson, "Parallel Trade in Pharmaceuticals" July 2003, p. 10.

price markets is substantial and the market of sufficient size to provide an attractive margin for the trader net of the cost of licensing, compliance, repackaging, shipment, and distribution. Traders can then price the imported drug enough below the locally-sourced drug to capture market share. Traders are motivated to provide only as much of the surplus to consumers and insurers, and to pharmacists (through discounts) as is needed to acquire market share.

The 2004 study of 6 countries found that most of the financial benefit from parallel importation was realized by the parallel traders. The study calculated that out of the total loss of manufacturer surplus (estimated at € 755 million in the retail brand market in the 6 countries), 85 to 95 percent accrued to parallel traders, while only between 5.9 and 13.2 percent accrued to health insurance organizations, and about 1 percent accrued to pharmacists. Overall, gross profits to parallel traders were 16 times as great as the savings to health insurance.[2]

Parallel Trade Provides Few Benefits to Patients and Health Insurers

Government's assumption in allowing and encouraging parallel trade is that it will provide benefits in the form of savings to the ultimate payers for health care – patients and health insurers. It is intended that parallel trade will have the effect of reallocating a portion of pharmaceutical manufacturer surpluses to payers in importing countries.

Evidence suggests, however, that only a small portion of pharmaceutical manufacturers' surpluses in Europe are reallocated through parallel trade to payers. Instead, most of the surplus is transferred from manufacturers (where it could support innovation) to intermediaries simply for the purpose of moving drugs across borders. Most of the surplus is consumed in transaction cost (including costs of relabeling, repackaging, and transporting) and parallel-importer profits. A small portion of the surplus is retained by pharmacies in the form of discounts in those countries where discounts are possible and where the government does not "clawback" pharmacy savings.

The pharmaceutical industry study of sales of imported drugs in Germany found that health insurance funds saved about € 60 million in 2001 – or about 0.3 percent of total pharmaceutical spending -- as a result of lower prices of imports.[3] The savings by health insurance funds is surprisingly small in light of German laws requiring substitution of low-priced alternatives for brand drugs and requiring that imported drugs account for 7 percent of pharmacy sales.

The 2004 study of 6 countries found that overall savings to health insurance organizations from parallel trade was 0.8 percent of total retail brand sales.[4] This savings increased to 1.8 percent when government "clawbacks" (mandatory transfers of savings from pharmacists to the government) were included. The study found that patients did not benefit directly from parallel trade, since they were covered by health insurance, although health insurance savings could benefit them indirectly. Pharmacies were found in many countries to have no incentive to dispense parallel imports, although there were modest financial benefits for pharmacies in other countries that had incentives to dispense parallel import drugs or did not limit pharmacy margins.

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[2] Panos Kanavos, et al. "The Economic Impact of Pharmaceutical Parallel Trade in European Union Member States: A Stakeholder Analysis," London School of Economics and Political Science, January 2004.
[3] Verband Forshender Arzneimittelhersteller (VFA) (2002), p. 4.
[4] Kanavos, et al., (2004).

The empirical studies of the effects of parallel trade within the EU support some general conclusions about the short-term and long-term effects of parallel trade that have been seen thus far:

- Pharmaceutical manufacturers experience a significant loss of market share for a small number of high-volume brand name drugs in importing countries as a result of parallel trade. These are the very drugs that provide the bulk of manufacturer revenues to support research and development.
- Retail price differences within a country between locally-sourced and parallel-traded drugs tend to be small.
- Payers in general – and health insurance organizations in particular in Europe -- benefit comparatively little from parallel trade.
- Patients in Europe do not benefit directly from parallel trade.
- Pharmacists benefit relatively little, depending on the structure of incentives and whether there is an opportunity to retain discounts.
- Parallel trade incurs transaction costs (including trader's profits) that add no value to products and serve largely to correct inefficiencies in supply created by the retention of heterogeneous price control systems in a common market.
- In the short term, the main consequence of parallel trade is to transfer most of the pharmaceutical manufacturers' margin in importing countries to parallel traders. There is a social welfare loss from the diversion of manufacturer surpluses, which might otherwise finance research and development.
- This could lead in the long-run to a net loss of social welfare in importing countries if small cost gains are outweighed by substantial losses in pharmaceutical innovation.

European parallel trade is characterized by some fundamental differences from the U.S. that suggest that even the modest savings achieved in the EU would not be realized in an importation program in the U.S. For example, the EU has a much lower need to ensure drug safety in a system of parallel trade, largely because it maintains a common standard for registry. As a result, regulation of parallel importers is fairly simple – with a requirement for licensure similar to standards for wholesalers, since parallel traders in this context operate like wholesalers – relabeling, storing, and transporting drugs.

Due to the need for more substantial safety measures and transportation and distribution activities, parallel trade into the U.S. would be more expensive, less profitable for traders, and, most likely, would generate even lower savings for health insurers and consumers. These findings are consistent with the Congressional Budget Office's report concluding that drug importation would have only a modest impact on prescription costs.[5]

IMPORTATION WILL NEGATIVELY IMPACT RESEARCH AND DEVELOPMENT

The fixed costs for the research-based pharmaceutical industry are primarily R&D costs. The U.S.-based pharmaceutical industry spends a higher percent of its sales on R&D than most industries - about 17.7% compared to an average of 4% for all other U.S. industries.[6,7] The

[5]Baker, Colin. "Would Prescription Drug Importation Reduce U.S. Drug Spending?" Congressional Budget Office – *Economic and Budge Issue Brief.* April 29, 2004.
[6] R&D Overview. www.phrma.org (2004)

Pharmaceutical Research and Manufacturers of America reported that in 2003, PhRMA member companies invested $33.2 billion in research and development for new pharmaceutical and biotechnology products.[8] Those investments yielded 21 new chemical entities and 14 new biological products in 2003 - most representing over 10 years of research and development to achieve FDA approval. For every 5000 molecules discovered, typically only 5 or 0.1% are suitable candidates for further study in clinical trials which, in turn, typically lead to only one successful product entering the market.[9]

R&D for the pharmaceutical industry represents a global joint cost. The value of the investments in research and development apply globally. Pharmaceutical companies cannot direct advances in medicine to particular markets. Global joint costs also occur in primary production when a plant in one country may supply compounds for manufacture in many countries. The joint costs for pharmaceutical development are usually committed well in advance of product launch and price negotiation.

Most industries that are subject to government rate-setting (such as utilities) have their fixed capital costs confined in the geographic area within which the rates apply and are therefore able to recover these costs through the rates. These costs are considered by regulators to be part of the base on which rates are determined, so that investments in infrastructure are easily recaptured through rate adjustments. Failure to set high enough rates hurts only the capital investment in that geographic area.

In contrast, the pharmaceutical industry (and ultimately, the patient) suffers globally when prices are set at levels that prevent sufficient reinvestment in joint global costs (i.e., research and development). With global fixed costs and national pricing, each separate national purchaser of pharmaceuticals has an incentive to free-ride by paying only their user-specific marginal cost. Monopoly government purchasers have the leverage to drive prices down to the level of country-specific marginal costs. Each country may thus decide to pursue its own self-interest, to the long-term detriment of pharmaceutical research and development globally, but with no immediate, divisible loss to that country.

With parallel trade, the prices available in low-cost countries can be diffused into other countries, eroding global revenues that are otherwise used to fund research and development. Parallel trade effectively transfers surplus revenues from research-based companies to parallel traders. Money, once available for research, is instead directed into the industry of parallel traders. Over time, this either drives prices up or reduces the margin manufacturers can sustain for low-cost countries. Innovation is starved for capital.

IMPORTATION RAISES LIABILITY ISSUES FOR MANUFACTURERS AND OTHERS IN THE DISTRIBUTON CHAIN

As FDA and numerous health and policy experts have recognized, the importation of prescription drugs increases the risks to patients of misbranding, adulteration, counterfeiting,

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[7] Patricia Danzon. "The Economics of Parallel Trade." *Pharmacoeconomics* 13(3): 293-304. March 1998.
[8] "Pharmaceutical Companies Receive FDA Approval for 35 New Medicines in 2003; Invest an Estimated $33.2 Billion in R&D." www.phrma.org. January 22, 2004.
[9] "Why Do Prescription Drugs Cost So Much and Other Questions About Your Medicines." PhRMA Publications. (2000)

contamination, and lack of adequate warnings or directions. Any litigation associated with imported products will likely result against those entities in the pharmaceutical distribution chain, including manufacturers, exporters, repackagers, importers, distributors, physicians and pharmacies. Patients may also sue state and local governments implementing programs for the importation of drugs. The risk may be especially high for manufacturers and other domestic elements of the distribution chain, since state and local governments as well as those foreign pharmacies and internet services that typically fill prescription drug orders from U.S. residents often disclaim all liability to the patient. Furthermore, some Canadian pharmacies and internet services have required that any dispute concerning drug products sold be resolved in Canadian courts under Canadian law, subjecting pharmaceutical manufacturers to extraterritorial reach.

IMPORTATION COMPROMISES A PRIMARY FUNCTION OF TRADEMARK AND COPYRIGHT PROTECTION

U.S. trademarks provide an indicator of source and a guarantee of quality of the product. Drug importation could violate the U.S. owner's trademark rights by compromising the primary functions of a trademark, namely source and quality guarantee. If the product is imported from a different source than is intended by the owner or if the quality of the product is different, then the U.S. trademark owner's right has been infringed under the U.S. trademark laws. Importation opens the door for compromises in quality at additional levels that are beyond the control of the US trademark owner, such as storage, handling, batch tracking and expiration dating.

ANTI-COUNTERFEITING TECHNOLOGIES WILL NOT PROVIDE A SUFFICIENT SAFETY GUARANTY

The use of certain covert and overt anti-counterfeiting technologies such as Radio Frequency Identification Device (RFID) and Dip Pen Nanolithography (DPN) could improve our ability to detect products that are manufactured illegitimately. The use of such track or trace technologies, especially in tandem, could contribute to the safety of products. In addition, proactively utilizing covert and overt "markers" could minimize the liabilities associated with adverse events experienced by patients receiving counterfeit products introduced into the U.S. healthcare system.

However, limited experience with anti-counterfeiting devices has exposed problems. Anecdotal data suggest that an authenticity problem exists. Currently, the distribution system has no systematic way of detecting when or how many consumers have already unwittingly taken a tainted product, either receiving no benefit or suffering ill-effects. Similarly, there is no way to calculate the quantity of illicit product that exists in the distribution chain.

In order to completely secure the U.S. drug supply from the manufacturer to the consumer, mass serialization of each packaged unit would be required. The retailer would need to authenticate the product at the point of dispensing to the consumer, thus eliminating the tainted product from the supply chain before consumption. There are many issues that must be addressed before mass serialization of packaged units can be effectively implemented (i.e., development of common standards, data ownership and sharing data issues, reduction in the cost to implement throughout the supply chain, etc.). Creating and implementing this complex system will take many years and extensive resources. The costs associated with instituting an anti-counterfeiting strategy are

Initiating anti-counterfeiting measures will not result in "guaranteed import security." The pharmaceutical industry and FDA must be prepared for the very likely probability that those individuals responsible for producing the counterfeit products will in time devise ways of circumventing the anti-counterfeiting technologies. Current estimates suggest that it takes six months for these technologies to be replicated or to be circumvented with reverse engineering.

The World Health Organization (WHO) reported that counterfeit drugs accounted for nearly 16.4% of all drugs produced in the international community.[10] The flexibility in trade regulations for drug importation will facilitate the need for greater international regulatory authority to control counterfeit drugs. As increased illicit manufacture of drugs continues, there will be greater strain on global health care infrastructure and access to safe medicinal products. The WHO issued a report in 1999 outlining those global factors contributing to counterfeit drugs including "lack of legislation prohibiting counterfeit drugs; weak penal sanctions; weak or absent national drug regulatory authorities; weak enforcement of drug laws; shortage/erratic supply of drugs; lack of control on drugs for export; trade involving several intermediaries and free trade zones; and corruption and conflict of interest."[11] FDA would need appropriate authority and sufficient funding to address these issues that will undoubtedly surface with the implementation of an importation program.

CONCLUSION

Schering-Plough considers access to pharmaceutical products both by our senior citizens and the 44 million uninsured Americans to be a critical public health issue. We do not believe this problem can be resolved simply through the importation of pharmaceutical product into the U.S. healthcare system. Maintaining the integrity of our pharmaceutical distribution system is paramount to ensuring the safety, quality and effectiveness of medicines in the U.S. Importation represents a tenuous solution to a complex issue without providing substantial cost savings. Allowing importation of pharmaceutical products will only escalate a rapidly growing problem of counterfeit products.

The pharmaceutical industry prides itself on the discovery and development of new and innovative therapies to diagnose, prevent and treat a multitude of medical conditions. We believe allowing importation will only stifle future medical advances by depleting the funding necessary to support our research and development. Tomorrow's cures will be sacrificed for today's limited savings. We need to continue investing in our product development to ensure a healthier future for all Americans and further those national policies enabling broader access to prescription drugs.

Sincerely,

Thomas J. Sabatino, Jr.
Executive Vice President & General Counsel

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[10] "Counterfeit Medicines: Overview." www.who.org (2004)

[11] "Counterfeit Drugs – Guidelines for the Development of Measures to Combat Counterfeit Drugs." World Health Organization (1999)